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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/677,240      | 10/03/2003  | Dan Peters           | 2815-0243P          | 9109             |

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EXAMINER

KIFLE, BRUCK

|          |              |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1624

DATE MAILED: 07/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                                       |                                      |  |
|------------------------------|---------------------------------------|--------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/677,240  | <b>Applicant(s)</b><br>PETERS ET AL. |  |
|                              | <b>Examiner</b><br>Bruck Kifle, Ph.D. | <b>Art Unit</b><br>1624              |  |

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 June 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,4-7 and 12-14 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,4-7 and 12-14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☒ Certified copies of the priority documents have been received in Application No. 09/528,176.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |                                                                                                                                                        |                                                                                         |
|--------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                                                            | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>10/03, 1/04, 6/04</u> . | 6) <input type="checkbox"/> Other: _____                                                |

***Election/Restriction***

Applicant's election of the species 1-(5-ethoxy-3-pyridyl)-methylnpiperazine is acknowledged. In view of Applicant's amendments to the claims, the restriction requirement is no longer applicable. Applicants limited R<sup>1</sup> to 3-pyridyl.

***Claim Rejections - 35 USC § 112***

Claims 1, 4-7 and 12-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- i) The term "cycloalkyl" is indefinite because it is not known how many atoms make up the ring or what kind of a ring is intended (monocyclic, bicyclic, spiro, fused, bridged, saturated, etc.). A clarification is required.
- ii) In claim 12 one skilled in the art cannot say which disease is responsive to the activity of nicotinic ACh receptor modulators and which disease is not responsive thereto. That is, one skilled in the art cannot say who is need thereof and who is not.
- iii) Regarding claim 12, the phrase "including human" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 12-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling as a method of treating a person suffering from nicotine withdrawal, does not reasonably provide enablement for treating all of the others recited in the claims

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In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Claim 12 is drawn to a method of treating a disease which is responsive to the activity of nicotinic ACh receptor modulation. Claims 13 and 14 are drawn to a method of treating of diseases in the central and peripheral system, a disease caused by smooth muscle contraction, neurodegeneration, inflammation, chemical substance abuse or withdrawal caused by the cessation of intake of chemical substances, such as smoking cessation and claim 14 is drawn to a method of treating Alzheimer's disease, Parkinson's disease, memory dysfunction and attention deficit hyperactivity disorder.

2) The state of the prior art: There are no known compounds of similar structure which have been demonstrated to treat any and all of the diseases recited. For example, there is no compound that can be used to treat chemical substance abuse or withdrawal caused by the cessation of intake of chemical substances generally. The notion that a compound could be effective against chemical substance abuse or withdrawal caused by the cessation of intake of chemical substances in general is absolutely contrary to our current understanding of how chemical dependencies operate. There is not, and probably never will be, a pharmacological treatment for "chemical substance abuse or withdrawal caused by the cessation of intake of chemical substances" generally. That is because "chemical substance abuse or withdrawal caused by the cessation of intake of chemical substances" is not a single disease or cluster of related disorders, but in fact, a

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collection with relatively little in common. Addiction to barbiturates, alcohol, cocaine, opiates, amphetamines, benzodiazepines, nicotine, etc. all involve different parts of the CNS system; different receptors in the body. For example, cocaine binds at the dopamine reuptake transmitter. Heroin addiction, for example, arises from binding at the opiate receptors, cigarette addiction from some interaction at the nicotinic acid receptors, many tranquilizers involve the benzodiazepine receptor, alcohol involves yet another system, etc. All attempts to find a pharmaceutical to treat chemical addictions generally have thus failed.

Alzheimer's disease is treated, albeit not successfully, using acetylcholine esterase inhibitors and Parkinson's disease using dopamine receptors. A disease in the central or peripheral system is not a single disease but embraces disease that are not related or even "opposites"; tumors and non-tumors are covered and diseases that are not treatable pharmacologically are also embraced (e.g. Down's syndrome).

3) The predictability or lack thereof in the art: It is presumed in the treatment of the diseases claimed herein there is a way of identifying any and all of the diseases which are responsive to the activity of nicotinic ACh receptor modulators. There is no evidence of record which would enable the skilled artisan in the identification of the diseases treatable with the disorders claimed herein. Regarding claim 12, the Supreme Court said in *Brenner v. Manson*, 148 USPQ at 696: "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." As U.S. Court of Customs and Patent Appeals stated *In re Diedrich* 138 USPQ at 130, quoting with approval from the decision of the board: "We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the

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statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.”

The how to use portion of the statute has not been addressed. This means that Applicants must teach the skilled practitioner, in this case a physician, how to treat a given subject. The physician clearly must know what disease and what symptoms is to be treated. In a case concerning the patentability of compounds with “good effects against a wide range of insects” *In re LORENZ AND WEGLER*, 134 USPQ 312 U.S. Court of Customs and Patent Appeals upheld the rejection of compound claims, noting that “[a]ppellants are seeking a seventeen year monopoly. We would remind them that if they have in truth invented something which promotes the progress of science and the useful arts, then in exchange for a patent grant they must make a full and complete disclosure of their invention, leaving nothing to speculation or doubt. That Congress so intended is evident from the strong and comprehensive language of Section 112 which appellants here have failed to satisfy.” In this case, Applicants have not provided what is being treated by claim 12, who the subject is, how one can identify said subject (i.e. how one can identify a subject in need), given no specific dose, given no specific dosing regimen, given no specific route of administration, and do not specify what diseases or symptom they intend to treat.

Also, it is presumed in the treatment of the diseases claimed herein there is a way of identifying any and all of the diseases which are responsive to the activity of nicotinic ACh

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receptor modulators. There is no evidence of record which would enable the skilled artisan in the identification of the diseases treatable with the disorders claimed herein. The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan for the many reasons stated above.

4) The amount of direction or guidance present and 5) the presence or absence of working examples: There are no doses present for treatment of the disorders recited.

6) The breadth of the claims: The claims are drawn to disorders that are not related and whose treatment is unknown.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan for the many reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jain et al. (J. Med. Chem (1967), 10(5), 812-8)). The reference teaches the compounds number 26, 27, 46 and 47 on

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Table II on page 814. These compounds differ from the claimed compound by having instant R<sup>1</sup> as 2-pyridyl and 4-pyridyl over the claimed 3-pyridyl. i.e., by being ring position isomers.

Position isomers are well established as being prima facie structurally obvious. See: Ex parte Engelhardt, 208 USPQ 343, 349; In re Mehta, 146 USPQ 284; In re Surrey, 138 USPQ 67; Ex parte Ulliyot 103 USPQ 185; Ex parte Naito 168 USPQ 437, 439; In re Norris 84 USPQ 459; Ex parte Allais 152 USPQ 66; Ex parte Henkel 130 USPQ 474; Ex parte Biel 124 USPQ 109; In re Crownse 150 USPQ 554; In re Fouche 169 USPQ 431; Ex parte Ruddy 121 USPQ 427; In re Wiechert 152 USPQ 249.

For example "Position Isomerism has been used as a tool to obtain new and useful drugs" (Engelhardt), and Position isomerism is a fact of close structural similarity" (Mehta, emphasis in the original).

Applicants are advised of MPEP 803.02 Restriction - Markush Claims [R - 2], fourth and fifth paragraph, where is stated:

"As an example, in the case of an application with a Markush - type claim drawn to the compound C - R, wherein R is a radical selected from the group consisting of A, B, C, D, and E, the examiner may require a provisional election of a single species, CA, CB, CC, CD, or CE. The Markush - type claim would then be examined fully with respect to the elected species and any species considered to be clearly unpatentable over the elected species. If on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush - type claim and claims to the elected species shall be rejected, and claims to the non - elected species would be held withdrawn from further consideration. As in the prevailing practice, **a second action on the rejected claims would be made final.**" (emphasis added).

On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is found that anticipates or renders obvious the Markush-type claim with respect to a non-elected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders

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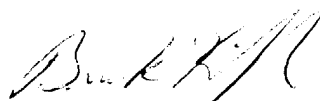
obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle, Ph.D. whose telephone number is 571-272-0668.

The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund J. Shah can be reached on 571-272-0674. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.



Bruck Kifle, Ph.D.  
Primary Examiner  
Art Unit 1624

BK  
July 16, 2004